

WHAT IS CLAIMED IS:

1. A method for identifying a bioactivity or a biomolecule of interest, comprising:
 - (a) contacting a library containing a plurality of clones comprising polynucleotides derived from a mixed population of organisms or more than one organism, with at least one oligonucleotide probe labeled with a detectable molecule; and
 - (b) separating clones with an analyzer that detects the detectable molecule.
2. The method of claim 1 further comprising:
 - (a) contacting the separated clones with a reporter system that identifies a polynucleotide encoding a bioactivity or biomolecule of interest; and
 - (b) identifying clones capable of modulating expression or activity of the reporter system thereby identifying a polynucleotide of interest.
3. The method of claim 1, wherein the library is an expression library.
4. The method of claim 1, wherein the detectable molecule is a fluorescent molecule.
5. The method of claim 1, wherein the analyzer is a FACS analyzer.
6. The method of claim 1, wherein the mixed population of organisms is from an environmental sample.
7. The method of claim 1, wherein the mixed population of organisms comprises microorganisms.
8. The method of claim 6, wherein the environmental sample contains extremophiles.

9. The method of claim 8, wherein the extremophiles are selected from the group consisting of hyperthermophiles, psychrophiles, halophiles, psychrotrophs, alkalophiles, and acidophiles.

10. The method of claim 2, wherein the reporter system is a bioactive substrate.

11. The method of claim 10, wherein the bioactive substrate comprises C12FDG.

12. The method of claim 11, wherein the bioactive substrate further comprises a lipophilic tail.

13. The method of claim 1, further comprising prior to (a):
(i) obtaining polynucleotides from a mixed population of organisms; and
(ii) generating a polynucleotide library.

14. The method of claim 13, further comprising normalizing the polynucleotides prior to generating the library.

15. The method of claim 1, wherein the clones are encapsulated in a microenvironment.

16. The method of claim 15, wherein the microenvironment is selected from beads, high temperature agaroses, gel microdroplets, cells, ghost red blood cells, macrophages, or liposomes.

17. The method of claim 16, wherein the clones are encapsulated in a gel microdroplet.

18. The method of claim 1, wherein the polynucleotide of interest encodes an enzyme.

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19. The method of claim 18, wherein the enzyme is selected from the group consisting of lipases, esterases, proteases, glycosidases, glycosyl transferases, phosphatases, kinases, mono- and dioxygenases, haloperoxidases, lignin peroxidases, diarylpropane peroxidases, eposize hydrolases, nitrile hydratases, nitrilases, transaminases, amidases, and acylases.
20. The method of claim 1, wherein the reporter system comprises a detectable label.
21. The method of claim 1, wherein the reporter system comprises a first test protein linked to a DNA binding moiety and a second test protein linked to a transcriptional activation moiety, wherein modulation of the interaction of the first test protein linked to a DNA binding moiety with the second test protein linked to a transcription activation moiety results in a change in the expression of a detectable protein.
22. The method of claim 1, wherein the polynucleotide of interest encodes a small molecule.
23. The method of claim 1, wherein the polynucleotide of interest, or fragments thereof, comprise one or more operons, or portions thereof.
24. The method of claim 23, wherein the operons, or portions thereof, encodes a complete or partial metabolic pathway.
25. The method of claim 24, wherein the operons or portions thereof encoding a complete or partial metabolic pathway encodes polyketide syntheses.
26. The method of claim 1, wherein the fluorescent analyzer is a fluorescence activated cell sorting (FACS) apparatus.

27. A method for identifying a polynucleotide encoding a polypeptide of interest comprising:
 - co-encapsulating in a microenvironment a plurality of library clones containing DNA obtained from a mixed population of organisms, with a mixture of oligonucleotide probes comprising a fluorescence marker and at least a portion of a polynucleotide sequence encoding a polypeptide of interest having a specified bioactivity under such conditions and for such time as to allow interaction of complementary sequences; and
 - identifying clones containing a complement to the oligonucleotide probe encoding the polypeptide of interest by separating clones with a fluorescent analyzer that detects fluorescence.
28. A method for high throughput screening of a polynucleotide library for a polynucleotide of interest that encodes a molecule of interest, comprising:
 - (a) contacting a library containing a plurality of clones comprising polynucleotides derived from a mixed population of organisms with a plurality of oligonucleotide probes labeled with a fluorescence molecule; and
 - (b) separating clones with a fluorescent analyzer that detects fluorescence.
29. The method of claim 28, further comprising:
 - (a) contacting the separated clones with a reporter system that identifies a polynucleotide encoding the molecule of interest; and
 - (b) identifying clones capable of modulating expression or activity of the reporter system thereby identifying a polynucleotide of interest.
30. The method of claim 28, wherein the library is an expression library.
31. The method of claim 28, wherein the mixed population of organisms is from an environmental sample.

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32. The method of claim 28, wherein the mixed population of organisms comprises microorganisms.
33. The method of claim 32, wherein the environmental sample contains extremophiles.
34. The method of claim 33, wherein the extremophiles are selected from the group consisting of hyperthermophiles, psychrophiles, halophiles, psychrotrophs, alkalophiles, and acidophiles.
35. The method of claim 29, wherein the reporter system is a bioactive substrate.
36. The method of claim 35, wherein the bioactive substrate comprises C12FDG.
37. The method of claim 36, wherein the bioactive substrate further comprises a lipophilic tail.
38. The method of claim 28, further comprising prior to (a):
 - (i) obtaining polynucleotides from a mixed population of organisms; and
 - (ii) generating a polynucleotide library.
39. The method of claim 38, further comprising normalizing the polynucleotides prior to generating the library.
40. The method of claim 28, wherein the clones are encapsulated in a gel micropipet.
41. The method of claim 28, wherein the polynucleotide of interest encodes an enzyme.
42. The method of claim 41, wherein the enzyme is selected from the group consisting of lipases, esterases, proteases, glycosidases, glycosyl transferases,

phosphatases, kinases, mono- and dioxygenases, haloperoxidases, lignin peroxidases, diarylpropane peroxidases, eposize hydrolases, nitrile hydratases, nitrilases, transaminases, amidases, and acylases.

43. The method of claim 29, wherein the reporter system comprises a detectable label.
44. The method of claim 28, wherein the reporter system comprises a first test protein linked to a DNA binding moiety and a second test protein linked to a transcriptional activation moiety, wherein modulation of the interaction of the first test protein linked to a DNA binding moiety with the second test protein linked to a transcription activation moiety results in a change in the expression of a detectable protein.
45. The method of claim 28, wherein the polynucleotide of interest encodes a small molecule.
46. The method of claim 28, wherein the polynucleotide of interest, or fragments thereof, comprise one or more operons, or portions thereof.
47. The method of claim 46, wherein the operons, or portions thereof, encodes a complete or partial metabolic pathway.
48. The method of claim 47, wherein the operons or portions thereof encoding a complete or partial metabolic pathway encodes polyketide syntheses.
49. The method of claim 28, wherein the fluorescent analyzer is a fluorescence activated cell sorting (FACS) apparatus.
50. The method of claim 28, wherein the plurality of oligonucleotide probes have different nucleic acid sequences.

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51. The method of claim 50, wherein the sequences are portions of a polynucleotide encoding a molecule of interest.
52. The method of claim 28, wherein the plurality of oligonucleotide probes have the same nucleic acid sequence.
53. A method of screening for a polynucleotide encoding an activity of interest, comprising:
 - (a) obtaining polynucleotides from an environmental sample;
 - (b) normalizing the polynucleotides obtained from the sample;
 - (c) generating a library from the normalized polynucleotides;
 - (d) contacting the library with a plurality of oligonucleotide probes comprising a fluorescent marker and at least a portion of a polynucleotide sequence encoding a polypeptide of interest having a specified activity to select library clones positive for a sequence of interest; and
 - (e) selecting clones with a fluorescent analyzer that detects fluorescence.
54. The method of claim 53, further comprising:
 - (a) contacting the selected clones with a reporter system that identifies a polynucleotide encoding the activity of interest; and
 - (b) identifying clones capable of modulating expression or activity of the reporter system thereby identifying a polynucleotide of interest; wherein the positive clones contain a polynucleotide sequence encoding an activity of interest which is capable of catalyzing the bioactive substrate.
55. A method for screening polynucleotides, comprising:
 - (a) contacting a library of polynucleotides wherein the polynucleotides are derived from a mixed population of organism with a probe oligonucleotide labeled with a fluorescence molecule, which fluoresce

upon binding of the probe to a target polynucleotide of the library, to select library polynucleotides positive for a sequence of interest;

- (b) separating library members that are positive for the sequence of interest with a fluorescent analyzer that detects fluorescence; and
- (c) expressing the selected polynucleotides to obtain polypeptides.

56. The method of claim 55, further comprising:

- (a) contacting the polypeptides with a reporter system; and
- (b) identifying polynucleotides encoding polypeptides capable of modulating expression or activity of the reporter system.

57. A method for obtaining an organism from a mixed population of organisms in a sample comprising:

- (a) encapsulating in a microenvironment at least one organism from the sample;
- (b) incubating the encapsulated at least one organism under such conditions and for such a time to allow the at least one microorganism to grow or proliferate; and
- (c) sorting the encapsulated at least one organism by flow cytometry to obtain an organism from the sample.

58. The method of claim 57, wherein the mixed population of organisms is from an environmental sample.

59. The method of claim 57, wherein the mixed population of organisms comprises microorganisms.

60. The method of claim 58, wherein the environmental sample contains extremophiles.

61. The method of claim 60, wherein the extremophiles are selected from the group consisting of hyperthermophiles, psychrophiles, halophiles, psychrotrophs, alkalophiles, and acidophiles.